

Amendment under 37 C.F.R. §1.116
U.S.S.N. 08/252,710

At page 59, line 25, delete "map of the MFG vector in table form."

In the claims:

Please cancel claim 3.

Please amend claims 1, 4, 10, 21, 44 as follows.

For the Examiner's convenience, all of the claims currently pending in the Application are listed below including those amended ("Amended"), non-amended ("Reiterated") and allowed ("Allowed").

1. (Four Times Amended) A recombinant retroviral vector useful to nonselectively transduce cells, comprising:

- (a) a 5' LTR derived from a retrovirus of interest;
- (b) a splice donor site located 3' to said 5' LTR;
- (c) a Psi packaging site located 3' to said splice donor site;
- (d) a [consensus] splice acceptor site located 3' to said Psi packaging site,

wherein said splice acceptor site is a splice acceptor site necessary for the generation of the env mRNA of a wild type retrovirus;

(e) an insertion site for a gene of interest located 3' to said [consensus] splice acceptor site;

(f) a 3' LTR derived from a retrovirus of interest located 3' to said insertion site; and wherein said vector does not contain a complete selectable marker gene used for the transduction of said cells, or a complete gag, env, or pol gene between said 5' and 3' LTRs.

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2. (Reiterated) A recombinant retroviral vector according to Claim 1, said vector further comprising, a portion of a *gag* coding sequence adjacent to said Psi packaging site.

4. (Twice Amended) A recombinant retroviral vector according to Claim [3] 2, said vector comprising a transcriptional promoter functionally positioned such that a transcript of a nucleotide sequence inserted into said insertion site is produced, wherein said transcript comprises a *gag* 5' untranslated region.

6. (Reiterated) A recombinant retroviral vector according to Claim 4, wherein said vector has all of the identifying characteristics of ATCC 68,754.

7. (Reiterated) A recombinant retroviral vector according to Claim 1, said vector further comprising a gene for expression inserted into said insertion site.

8. (Reiterated) A recombinant retroviral vector according to Claim 7, wherein said gene for expression is selected from the group consisting of: a hormone, an enzyme, and a receptor.

9. (Reiterated) A recombinant retroviral vector according to Claim 8, wherein the gene encodes factor VIII or tPA.

10. (Four Times Amended) A recombinant retroviral vector useful to nonselectively transduce cells, said vector comprising:

- (a) a 5' LTR derived from a retrovirus of interest;
- (b) a Psi packaging site located 3' to said 5' LTR;
- (c) a [consensus] splice acceptor site located 3' to said Psi packaging site, wherein said splice acceptor site is a splice acceptor site necessary for the generation of the env mRNA of a wild type retrovirus;
- (d) an alpha globin transcriptional promoter located 3' to said Psi packaging site;

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(e) an insertion site for a gene of interest located 3' to said alpha globin transcriptional promoter;

(f) a 3' LTR derived from a retrovirus of interest located 3' to said insertion site; and wherein said vector does not contain a complete selectable marker gene used for the transduction of said cells, or a complete *gag*, *env*, or *pol* gene between said 5' and 3' LTRs.

11. (Reiterated) A recombinant viral vector according to Claim 10, said vector further comprising, a portion of the 5' untranslated region of the alpha-globin gene that is naturally joined to said alpha globin transcriptional promoter.

12. (Reiterated) A recombinant retroviral vector according to Claim 11, said vector further comprising, an enhancer, wherein said enhancer is not in said 5' or 3' LTR.

13. (Reiterated) A recombinant retroviral vector according to Claim 12, wherein an enhancer sequence is located upstream from said transcriptional promoter.

14. (Reiterated) A recombinant retroviral vector according to Claim 13, wherein the enhancer sequence is a cytomegalovirus enhancer sequence.

15. (Reiterated) A recombinant viral vector according to Claim 14, wherein the vector has all of the identifying characteristics of ATCC 68755.

16. (Reiterated) A recombinant retroviral vector according to Claim 10, wherein said 3' LTR does not contain a functional enhancer sequence.

17. (Reiterated) A recombinant retroviral vector according to Claim 10, said vector further comprising, a gene for expression inserted into said insertion site.

18. (Reiterated) A recombinant retroviral vector according to Claim 19, wherein said gene for expression is selected from the group consisting of a hormone, an enzyme, and a receptor.

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19. (Reiterated) A recombinant retroviral vector according to Claim 18, wherein the gene encodes factor VIII or tPA.

20. (Reiterated) A recombinant retroviral cell line wherein said cell line has been transfected with the coding sequence of a retroviral vector of any one of Claim 1 to 19.

21. (Four Times Amended) A recombinant retroviral vector useful to nonselectively transduce cells, comprising, a 5' LTR derived from a murine leukemia virus, a [consensus] splice acceptor site and an insertion site for a gene of interest located between said 5' and 3' LTRs, wherein said splice acceptor site is a splice acceptor site necessary for the generation of the env mRNA of a wild type retrovirus, and wherein said vector does not contain a complete selectable marker gene used for the transduction of said cells, or a complete gag, env, or pol gene.

22. (Reiterated) The recombinant retroviral vector of Claim 21, further comprising an exogenous enhancer.

23. (Reiterated) The recombinant retroviral of Claim 22, wherein the exogenous enhancer is derived from a myeloproliferative sarcoma virus.

24. (Reiterated) The recombinant retroviral vector of claim 22, wherein the exogenous enhancer is derived from Moloney Friend Virus.

25. (Reiterated) The recombinant retroviral vector of claim 21, 22, 23, or 24, further comprising a B2 mutation.

26. (Reiterated) The recombinant retroviral vector of Claim 21, 22, 23, or 24, wherein the 3' LTR is replaced with a 3' LTR derived from a myeloproliferative sarcoma virus.

27. (Reiterated) The recombinant retroviral vector of Claim 26, further comprising a B2 mutation.

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28. (Reiterated) The recombinant retroviral vector of Claim 21, 22, 23, or 24, wherein the 5' LTR is replaced with a 5' LTR derived from a myeloproliferative sarcoma virus.

29. (Reiterated) The recombinant retroviral vector of claim 28, further comprising a B2 mutation.

30. (Reiterated) The recombinant retroviral vector of Claim 21, 22, 23, or 24, wherein both the 5' LTR and the 3'LTR are respectively replaced with a 5' LTR and a 3' LTR derived from a myeloproliferative sarcoma virus.

31. (Reiterated) The recombinant retroviral vector of Claim 30, further comprising a B2 mutation.

35. (Reiterated) A recombinant retroviral particle produced by a producer cell comprising the recombinant retroviral vector of claim 1 said particle having the property of being capable of transducing mammalian cells.

36. (Reiterated) A particle according to claim 35, 42, or 43 wherein said transducing occurs *in vitro*.

37. (Reiterated) A particle according to claim 35, 42, or 43 wherein said transducing occurs *in vivo*.

38. (Allowed) A new retroviral vector derived from the vector MFG having the identifying characteristics of ATCC 68,754.

39. (Allowed) A new retroviral vector derived from α -SGC having the identifying characteristics of ATCC 68,755.

40. (Allowed) A new retroviral vector derived from MFG having the identifying characteristics of ATCC 68,754, wherein said vector comprises the B2 mutation.

41. (Allowed) A new retroviral vector derived from α -SGC having the identifying characteristics of ATCC 68,755, wherein said vector comprises the B2 mutation.

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42. (Reiterated) A recombinant retroviral particle produced by a producer cell comprising the recombinant retroviral vector of claim 10, said particle having the property of being capable of transducing mammalian cells.

43. (Reiterated) A recombinant retroviral particle produced by a producer cell comprising the recombinant retroviral vector of claim 21, said particle having the property of being capable of transducing mammalian cells.

44. (Once Amended) A recombinant retroviral vector useful to nonselectively [transfect] transduce cells, comprising:

- [(g)] (a) a 5' LTR derived from a retrovirus of interest;
- [(h)] (b) a splice donor site located 3' to said 5' LTR;
- [(i)] (c) a Psi packaging site located 3' to said splice donor site;
- [(j)] (d) a [consensus] splice acceptor site [, derived] from [MOV- 9] MOV-9.1, located 3' to said Psi packaging site;
- [(k)] (e) an insertion site for a gene of interest located 3' to said splice acceptor site;
- [(l)] (f) a 3' LTR derived from a retrovirus of interest located 3' to said insertion site; and wherein said vector does not contain a complete selectable marker gene used for the [transfection] transduction of said cells, or a complete *gag*, *env*, or *pol* gene between said 5' and 3' LTRs.

In the Figures:

Please substitute amended informal Figures 1, 3, 7, 8, 9B, 10, 11A-C, 15, and 17 for the same as filed. (A copy of Applicants' letter to the Official Draftsperson requesting these amendments filed December 20, 1999 is enclosed herewith as Appendix A).

In Fig. 1, "3' ss" has been replaced with - - 3' ss - - and the letters made smaller.

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In Fig. 3, the typographical error, "Asp7" has been replaced with -- Asp718 --.

In Fig. 7, "VII" has been replaced with -- VIII --.

In Fig. 8, "α" has been replaced with -- αSGC --.

In Fig. 9B, "1056" has been replaced with -- 1036 --; "Xho2" has been replaced with -- XhoI -- (support for which can be found at page 29, lines 14-18 and in Fig. 9A (I); a -- C -- has been added to the sequence, second line, third nucleotide from the right (support for which can be found at page 30, line 1); and "8 bp" which is a typographical error has been replaced with -- 18 bp -- in the correct position between the indicators of XbaI and BamHI (support for which can be found in Fig. 9B at (V)).

In Fig. 10, "BAMGI" has been replaced with -- BAMHI --.

Figs. 11A, B, and C as originally filed have been replaced with Figs. 11A, B, and C enclosed herewith, and in which the "A", "B", and "C" designations are accurately placed and cross-hatching used.

In Fig. 15, "An3'" has been replaced with -- [A]_n 3' --.

In Fig. 17, the nucleotide numbering on the left hand side of the sequence has been restored.

REMARKS

At the outset, Applicants wish to thank the Examiner for the courtesy of the interview held on October 20, 1999. At that interview, the outstanding rejections and proposed amendments to the specification, claims, and drawings were discussed. Certain issues discussed at the interview will be described in detail below.

Reconsideration of the Application in view of the above amendments, the interview, and the following remarks is respectfully requested.

Claims 1-4, 6-31, and 35-44 are pending in this Application. Claims 38-41 have been allowed.